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Modelling the effect of infection prevention and control measures on rate of *Mycobacterium tuberculosis* transmission to clinic attendees in primary health clinics in South Africa

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ABSTRACT

Background Elevated rates of tuberculosis in healthcare workers demonstrate the high rate of *Mycobacterium tuberculosis (Mtb)* transmission in health facilities in high-burden settings. In the context of a project taking a whole systems approach to tuberculosis infection prevention and control (IPC), we aimed to evaluate the potential impact of conventional and novel IPC measures on *Mtb* transmission to patients and other clinic attendees.

Methods An individual-based model of patient movements through clinics, ventilation in waiting areas, and *Mtb* transmission was developed, and parameterised using empirical data from eight clinics in two provinces in South Africa. Seven interventions—codeveloped with health professionals and policy-makers—were simulated: (1) queue management systems with outdoor waiting areas, (2) ultraviolet germicidal irradiation (UVGI) systems, (3) appointment systems, (4) opening windows and doors, (5) surgical mask wearing by clinic attendees, (6) simple clinic retrofits and (7) increased coverage of long antiretroviral therapy prescriptions and community medicine collection points through the Central Chronic Medicine Dispensing and Distribution (CCMDD) service.

Results In the model, (1) outdoor waiting areas reduced the transmission to clinic attendees by 83% (IQR 76%–88%), (2) UVGI by 77% (IQR 64%–85%), (3) appointment systems by 62% (IQR 45%–75%), (4) opening windows and doors by 55% (IQR 25%–72%), (5) masks by 47% (IQR 42%–50%), (6) clinic retrofits by 45% (IQR 16%–64%) and (7) increasing the coverage of CCMDD by 22% (IQR 12%–32%).

Conclusions The majority of the interventions achieved median reductions in the rate of transmission to clinic attendees of at least 45%, meaning that a range of highly effective intervention options are available, that can be tailored to the local context. Measures that are not traditionally considered to be IPC interventions, such as appointment systems, may be as effective as more traditional IPC measures, such as mask wearing.

Key questions

What is already known?

- There are elevated rates of *Mycobacterium tuberculosis* (*Mtb*) transmission in healthcare facilities in high-burden settings.
- A range of infection prevention and control (IPC) measures exist, but estimates of their potential effects on transmission are limited.

What are the new findings?

- We estimate the potential effects of seven conventional and novel IPC interventions on *Mtb* transmission to patients in primary healthcare clinics in South Africa.
- The interventions are estimated to reduce the rate of transmission by 22%–83%, with six of the seven interventions achieving reductions of at least 45%.

What do the new findings imply?

- A range of highly effective intervention options are available, that can be tailored to the local context.
- Measures that are not traditionally considered to be IPC interventions, such as appointment systems, may be as effective as more traditional IPC measures, such as mask wearing.

INTRODUCTION

All else being equal, the risk of tuberculosis from transmission in primary healthcare (PHC) clinics is likely to be higher than in many other types of congregate settings, due to higher rates of clinic attendance both by people with infectious tuberculosis, and by people at high risk of progression to disease.[1] Evidence for high rates of *Mycobacterium tuberculosis* (*Mtb*) transmission in health facilities can be found in studies of infection or disease risk in healthcare workers, with a recent

systematic review finding an incidence of tuberculosis in healthcare workers in high burden countries 2–12 times higher than in the general population.[2]

The challenge of high rates of *Mtb* transmission in healthcare facilities comes with opportunities for control. Compared with many other putative high transmission risk congregate settings such as bars[3] or public transport,[4] healthcare facilities should be relatively accessible settings for infection prevention and control (IPC) interventions. Two recent reviews, however, have identified a number of barriers to the successful implementation of IPC measures in healthcare facilities, including lengthy, ambiguous or unclear guidelines; overwork; lack of training; lack of space and/or equipment and concerns about patient stigmatisation.[5 6] The *Umoya omuhle* ('good air' in isiZulu) project was designed to address these barriers, taking a multidisciplinary whole systems approach to understanding the drivers of *Mtb* transmission in PHC clinics in South Africa, and the individual and system constraints to implementing IPC measures.[7] The project combined quantitative and qualitative data collection, and used a system dynamics modelling approach[8] to identify potential IPC interventions. Interventions were selected that local policy-makers and health professionals, working at PHC and province levels (including PHC and district level healthcare workers), ranked highly in terms of both feasibility of implementation and perceived likely impact.[9]

To make informed and evidence-based decisions on the implementation of IPC measures in PHC clinics, it is necessary to know the likely effects of the interventions on transmission risk. Empirical data on intervention impact are limited however, and focus on risk to healthcare workers, and on hospital settings,[10] likely due to the difficulties in empirically evaluating changes in risk to patients and other clinic attendees. We therefore use mathematical modelling to fill this key information gap, using a model of patient movement through clinics and ventilation rates (informed by empirical data on both) to estimate the potential effects of the interventions on the rate of *Mtb* transmission to clinic attendees in PHC clinics in KwaZulu-Natal and Western Cape provinces, South Africa. In doing so, we provide information that is critical to policy-makers, to inform decisions on which intervention or interventions to implement in clinics.

METHODS

Clinic attendee movement data

Collection

Clinic attendee movement data were collected on a single day per clinic, in six PHC clinics in KwaZulu-Natal province in February–March 2019, and five in Western Cape in May 2019 (with the exception of one clinic in KwaZulu-Natal, where data were collected on two separate days).[11] Briefly, all patients and other clinic attendees (people attending with or on the behalf of patients) arriving at the clinic or present at the clinic at the start of data collection were given a unique barcode. Research staff with barcode scanners were positioned at key points throughout the clinic, including the facility entrance(s), the filing window where patients registered and collected their medical record, the triage/vitals station where measurements such as blood pressure were taken, and doorways of waiting areas and some consultation rooms. Each time that a clinic attendee passed through a doorway or visited a station (eg, the filing window) their barcode was scanned, recording the time and the location. This allowed the attendees' movements through the clinic to be tracked. Basic demographic information and information on visit reasons were collected from all attendees. Clinic staff were also assigned barcodes, and their movements tracked. Table 1 shows the number of attendees recorded at each clinic, the clinic opening time and the time and number of attendees present at the start and end of data collection.

Table 1 Clinic information

				Start of data collection		End of data collection	
	Clinic ID number	Number of attendees*	Clinic opening time	Time	Attendees present†	Time	Attendees present†
KwaZulu-Natal	1	417	07:00	07:11	130 (31%)	14:19	129 (31%)
	2	171	07:00	07:54	37 (22%)	14:08	47 (27%)
	5	349	07:00	07:45	69 (20%)	14:19	89 (26%)
	6	377	07:30	08:27	63 (17%)	14:02	34 (9%)
Western Cape	8	69	07:30	07:49	2 (3%)	14:04	11 (16%)
	9	120	07:30	08:31	44 (37%)	14:06	38 (32%)
	11	308	07:00	07:37	157 (51%)	14:51	43 (14%)
	12	144	07:30	07:59	39 (27%)	14:03	17 (12%)

Clinic ID numbers correspond to numbers used in other papers from the *Umoya omuhle* project.
*Number of patients and other clinic attendees included in the data collection.
†Number and proportion of all patients and other clinic attendees included in the data collection who were already present at the start of data collection, or still present at the end.

Full details of the data collection methods and results are given in Karat *et al*.[11]

Analysis

Data on clinic attendee movements were only collected from all main areas of the clinic in eight clinics, four in KwaZulu-Natal and four in Western Cape, and therefore only those clinics were considered in this work.

Attendees' movements through the clinic were simplified to four key stages/times: the time they arrived at the clinic, the time that they were first recorded at the filing window ('files'), the time that they were first recorded at the triage/vitals station ('vitals') and the time they left the clinic. All attendees were assumed to pass through each of the four stages, in order. These times were missing for many individuals, due to their barcode not being scanned, or their arrival or departure occurring outside the data collection period. Missing data on these times were imputed using multiple imputation (see online supplemental material for details). The times that attendees started consultations were also estimated, from the attendees' leaving times and data on mean consultation lengths.

Due to missing data on attendees' movements between waiting areas, attendees' waiting locations were also simplified, with each attendee assigned a single waiting area for each stage: waiting for files, waiting for vitals and waiting for any consultations (including the pharmacy). Waiting areas were assigned based on recorded barcode scans into and out of waiting areas, and knowledge of clinic space use (see online supplemental material for details).

In total, 40 baseline attendee datasets were created for each clinic, incorporating the uncertainty in the four times and three waiting locations.

Patient and public involvement

Methods used to collect and analyse patient flow data were developed through informal consultation with a range of stakeholders, including clinic managers and other healthcare workers and attendees at an Umoya omuhle workshop on patient flow and waiting times, which included patient representatives. The Umoya omuhle study was discussed with and approved by the Africa Health Research Institute's community advisory board prior to the finalisation of the protocol.

Ventilation and room size data

Data on ventilation rates were collected on 84 occasions from 57 rooms in 10 clinics in KwaZulu-Natal and Western Cape, using carbon dioxide (CO_2) release experiments and continuous CO_2 concentration data, with the room doors and windows in typical in-use configurations ('usual conditions'). Room measurements were also made, and room volumes calculated. Ventilation rates, measured in air changes per hour (ACH), were calculated for each room. Details are given in Deol *et al*.[12]

Figure 1 Example illustration of the movement of two hypothetical patients through a clinic in the model. The blue and green shadings indicate different waiting areas.

Data were also collected from 20 clinic rooms, with all windows and doors fully open ('maximum ventilation conditions'). The relative change in ACH in maximum ventilation conditions was calculated for each room, relative to the ACH in usual conditions in the same room on the same day.

Model

Clinic attendee movements

We developed an individual-based model that tracked the time at each stage for each clinic attendee (arrival, files, vitals and leaving), and the locations that they were waiting in between stages. Figure 1 illustrates the movement through the model for two hypothetical patients, and full details are given in the online supplemental material.

Transmission risk

Transmission risk was calculated using an approach based on the Wells-Riley equation[13], and assuming no saturation of infection risk between model time steps. Results are presented as relative reductions in risk only, due to the large amounts of uncertainty that exist in quanta production rates.[14] The estimated mean number of quanta ('infectious doses')[15] in each waiting area of the clinic was tracked over time, assuming that 1% of adult patients[16] and 0.02% of child patients[16–18] had potentially infectious tuberculosis. Estimates of ventilation rates were used to determine the rate at which quanta were cleared from the room. Cumulative infection risk over time was tracked both for each individual attendee, and by room. Overall infection risk was calculated as the sum of infection risk for all simulated clinic attendees, over all time they spent in clinic waiting areas.

Full details of the model and model parameterisation are given in the online supplemental material.

Interventions

Seven potential IPC interventions had been identified through qualitative research and system dynamics modelling workshops conducted as part of the *Umoya omuhle* project.[9] They were implemented individually in the model as follows:

1. *Opening windows and doors.* Ensuring windows and doors in waiting areas are kept open at all times. This was implemented in the model through increased ACHs, with the relative increase in each waiting area and model run sampled from a distribution fitted to the empirical ventilation data.

2. *Simple clinic retrofits*. Retrofits are changes to the building to improve ventilation rates. This could include installing lattice brickwork or whirlybird fans. Due to the large amount of variation between clinic spaces in the types of building retrofits that would be suitable, and the lack of sufficient data on the effects of the retrofits on ventilation rates in different types of spaces, we did not model specific retrofits or packages of retrofits. Instead, we simulated an undefined package of retrofits that are sufficient to increase ACH to a minimum of 12 in all rooms, chosen in line with WHO guidelines.[2 19]
3. *UVGI systems*. We assume in this intervention that appropriate and well-maintained ultraviolet germicidal irradiation (UVGI) systems are installed in all indoor clinic waiting areas. This was implemented in the model through an additional quanta clearance rate, equivalent to a ventilation rate of 24 ACH (95% CI 9.9 to 62).[20]
4. *Surgical mask wearing by clinic attendees*. Based on discussions with healthcare workers and professionals active in the management of health services in the two provinces we worked in, as well as review of qualitative data collected, we determined that a scenario where 70% of attendees wear surgical masks 90% of the time was plausible. This was implemented in the model as 63% of attendees wearing masks 100% of the time, with the attendees who wear the masks chosen at random each model run. Masks were assumed to reduce the rate of quanta production by 75% (95% CI 56% to 85%),[21] and have no effect on rate of infection for the person wearing the mask.[22]
5. *Increased CCMDD coverage*. South Africa's Central Chronic Medicine Dispensing and Distribution (CCMDD) programme is designed to allow patients with stable chronic health conditions to collect their medicines from convenient locations, such as local pharmacies.[23] This means that they do not need to queue at clinics unnecessarily. The purpose of this intervention is to increase the coverage of CCMDD and similar programmes for eligible patients on antiretroviral therapy (ART), and to ensure that pick-up points do not require patients to queue at clinics. We assumed that 92% (95% CI 84% to 95%) of patients could have their ART appointments reduced to once every 6 months,[24] and that the remaining 8% of people need monthly ART appointments. This was implemented in the model through removing 31% (IQR) 22%–34%) of patients attending for HIV care, chosen at random each model run.
6. *Queue management system with outdoor waiting areas*. Empirical data show that clinic waiting areas are often crowded, and that in many clinics, patients wait in unsuitable areas such as corridors.[11] Conversations with clinic staff suggested that this is partly due to patient concerns that if they wait in other areas, they may not hear their name being called, and may miss their turn. This intervention therefore combines a large, covered outdoor waiting area with a queue management system. We assumed that only 5–10 patients would be allowed to wait inside the clinic for each of the three stages, with the rest waiting in a large, covered, outdoor waiting area, with a very high ventilation rate of 52–70 ACH.[25]
7. *Appointment system*. In this intervention, we simulated an appointment system to reduce clinic overcrowding, through spacing out the arrival times of patients. As date-time appointment systems were already in place in some form in the Western Cape clinics on the day that the patient data were collected, we only modelled the appointment intervention in the KwaZulu-Natal clinics. We assumed that all patients aged <16 years and a proportion of patients with acute visit reasons would arrive at the clinic at the same time as in the baseline scenario, and be seen the same day. We assumed that all adult chronic patients, and a proportion of adult acute patients would be given appointments, with their arrival time spaced out between 9 am and 2 pm.

The CCMDD intervention reduces the number of patients, and the appointment system intervention changes the arrival times of some patients. Both these interventions may have consequences for the times that other patients are seen at each stage (files, vitals and consultations/leaving). The consequences are likely to vary by stage, and will vary depending on whether or not the stage is rate limiting. In other words, does the stage usually have the capacity to see patients as soon as they are ready, or are there usually queues? The model therefore contained two scheduling mechanism options per stage, which assume that the stage is or is not rate limiting.

Full details of the model and simulated interventions are given in the online supplemental material.

Model runs and uncertainty estimation

For each of the 40 patient datasets (incorporating the uncertainty in the times and waiting locations), 100 ventilation input sets were created, with the baseline ACH in each room varying between input sets. For each of the 4000 combinations, four different scheduling scenarios were simulated, assuming that the files and vitals stages are or are not rate limiting, in a two-by-two factorial design. Consultations/leaving was assumed to be a rate limiting stage in all the main model runs. This gave a total of 16 000 model runs for each clinic and intervention.

In addition to this, as a sensitivity analysis, an additional 16 000 model runs were done for each clinic and intervention, where it was assumed that consultations were not a rate limiting stage.

RESULTS

Effect of the interventions on the relative rate of transmission to patients

Figure 2 shows the estimated reduction in the rate of *Mtb* transmission to patients in each of the intervention scenarios, compared with the baseline scenario, overall and by province. Overall, in the model, opening windows

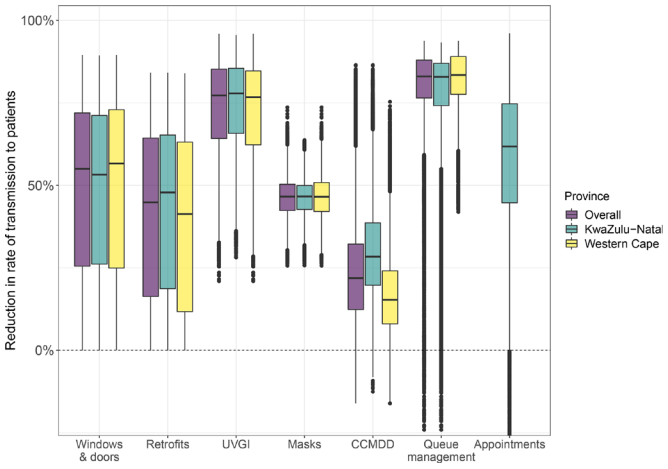

Figure 2 Estimated reduction in the rate of *Mycobacterium tuberculosis* transmission to patients in clinics, by province and intervention. The central line indicates the median, the box range the IQR, the whiskers the most extreme value within 1.5 * IQR from the box, and the points outlying values. In the queue management intervention in KwaZulu-Natal, 1.3% of points were below −20%, with a minimum of −162%. In the appointment system intervention in KwaZulu-Natal, 1.3% of points were below −20%, with a minimum of −83%. These points are not shown on the graph. The appointment system intervention was not modelled in Western Cape, due to the presence of existing appointment systems. CCMDD, Central Chronic Medicine Dispensing and Distribution; UVGI, ultraviolet germicidal irradiation.

and doors reduced the transmission rate by 55% (IQR 25%–72%), clinic retrofits by 45% (IQR 16%–64%), installing UVGI by 77% (IQR 64%–85%), surgical mask wearing by patients by 47% (IQR 42%–50%), increasing the coverage of CCMDD by 22% (IQR 12%–32%) and a queue management system plus outdoor waiting area by 83% (IQR 76%–88%). In the KwaZulu-Natal clinics, implementing an appointment system in the model reduced the transmission rate by 62% (IQR 45%–75%).

There was little variation in estimated impact by province, with the exception of increasing the coverage of CCMDD, where reductions in the transmission rate were higher in KwaZulu-Natal clinics (28% IQR 20%–39%) than in Western Cape clinics (15% IQR 8%–24%), reflecting the higher prevalence of HIV and higher ART coverage in KwaZulu-Natal.

Figure 3 shows the number of patients in the clinic 1 over time in the baseline scenario, then with the appointment system and the CCMDD intervention. The lower panels show the mean rate of transmission to each patient in the clinic over time in all scenarios. Similar figures for the other clinics are in the online supplemental material.

Sensitivity analyses

Simulating consultations as a non-rate limiting stage reduced the estimated reduction in the rate of transmission from 22% (IQR 12%–32%) to 15% (IQR 8.7%–23%) in the CCMDD scale-up intervention, and from 62% (IQR 45%–75%) to 24% (IQR 13%–47%) in the appointments intervention (online supplemental figure S3).

DISCUSSION

In this paper, we estimated the potential effects of seven interventions on the rate of *Mtb* transmission to patients

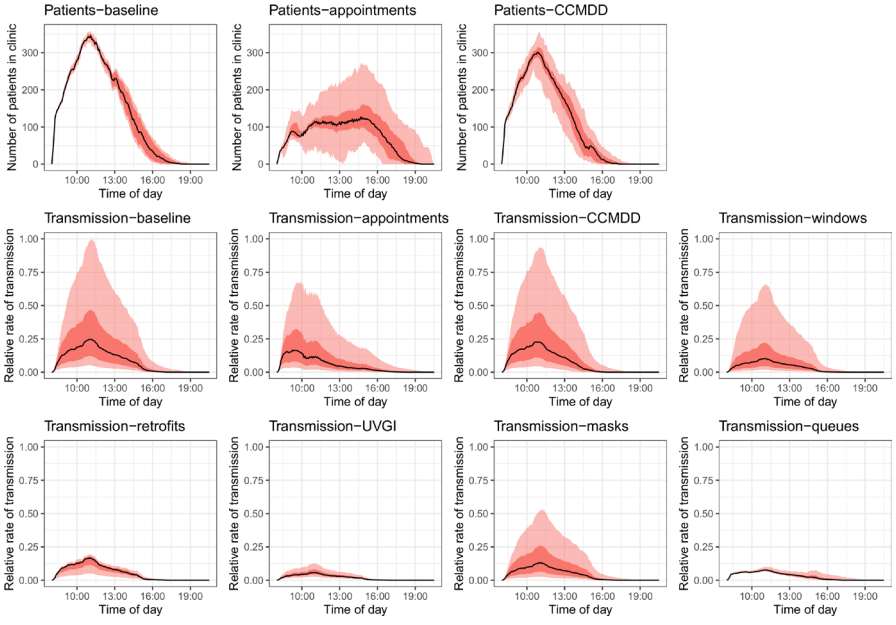

Figure 3 Number of patients in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each patient in the clinic over time in all scenarios, for clinic 1. The black line shows the median result, the dark red band the IQR and the light red band the 95% plausible range. For interventions where a plot of the number of patients over time is not shown, the intervention has no effect on patient numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. Figures for the other clinics are shown in the supplemental material. CCMDD, Central Chronic Medicine Dispensing and Distribution; UVGI, ultraviolet germicidal irradiation.

and other clinic attendees in PHC clinics in two provinces in South Africa. A queue management system with outdoor waiting areas and installing UVGI systems were identified as the most effective interventions, reducing the rate of transmission by an estimated 83% and 77%, respectively. The majority of interventions resulted in substantial reductions in the transmission rate however, demonstrating that a range of highly effective IPC measures exist. This includes appointment systems, which are not traditionally considered as IPC measures. This highlights the benefits of broadening our views of IPC and expanding our view of the population to be protected beyond healthcare workers, to also include patients and other clinic attendees.

Many of the interventions could be implemented in different ways in practice, increasing or decreasing their effects. For example, installing a more extensive package of retrofits, or taking measures to achieve a higher level of mask wearing. Combining interventions will also increase impact, although returns will diminish with multiple interventions. The COVID-19 pandemic may also have led to changes in the way that PHC clinics operate, some of which may last beyond the end of the epidemic. For example, the acceptability to clinic attendees of mask wearing may increase, increasing the coverage that can be achieved. When interpreting the results, consideration should therefore be given to any differences in the way that we implemented the intervention in the model, and the way that they would be implemented in a specific context. Nevertheless, our results provide a useful baseline estimate of the impacts and relative impacts of the different interventions.

The choice of IPC intervention(s) to implement at the clinic level, or to recommend at a district or provincial level, will necessarily also be guided by other factors. The costs of implementing and maintaining the different interventions will be a key factor, and is being explored in further work as part of the *Umoya omuhle* project. Guided by a whole systems approach, we have comprehensively costed the interventions proposed by also considering how to overcome potential system and practical barriers to implementation. The ease and practicality of implementation is also an important consideration, and will vary by clinic. For instance, is there sufficient space to install an outdoor waiting area? And is the climate suitable for interventions that increase natural ventilation rates? The systems dynamics modelling work conducted to identify the interventions simulated here also aimed to identify the mechanisms necessary to achieve the interventions. For instance, for ensuring an effective queue management programme, mechanisms such as community and health service staff consultation and creation of covered outdoor waiting areas were discussed.[9]

Some of the interventions have additional benefits to patients. Improving the coverage of CCMDD may be beneficial to patients stable on ART, reducing the amount of time they spend queuing at clinics and the financial cost to patients. An appointment system should also reduce the time spent at clinics for the majority of patients. The effect of the interventions on risk of transmission to healthcare workers and other clinic staff should also be considered. All the interventions described here will reduce risk to all staff situated in waiting areas, such as security guards and clerks in some clinics. Many of the interventions will also reduce risk to staff in consultation rooms, provided that the interventions are also implemented in those spaces. Interventions that reduce risk by reducing overcrowding in waiting areas (appointment systems, CCMDD scale-up and outdoor waiting areas) will have little effect on risk for staff based in consultation rooms however.

Finally, we estimate the effect of the interventions on an airborne infection, *M. tuberculosis*. The relative effects of the different interventions on other infections that spread primarily through airborne transmission, such as measles and chickenpox, are likely to be similar, although the concentration of these infections in children rather than adults may alter the effects slightly. The effects will differ, however, for infections where droplet or fomite transmission may play a larger role, such as SARS-CoV-2 and influenza. Fully exploring the impact on these infections is beyond the scope of this paper, however, as a rough guide, interventions that act through reducing patient concentrations (CCMDD and appointments systems) or reducing the release of pathogens (masks) will have a greater effect on these infections than interventions that act through improving ventilation (opening windows and doors, clinic retrofits, outdoor waiting areas) or air disinfection (UVGI).

There are a number of limitations to this work. First, empirical data on the flow of clinic attendees through clinics were only available for 1 day per clinic, meaning that we cannot disentangle variation between the simulated clinics in the intervention effects that arises from day-to-day variation within the clinic from that which arises from variation between clinics. For this reason, the results are presented by province only in the main results figure, rather than by clinic. Additional empirical data (both on patient movements and ventilation rates in waiting areas), and simulated clinic days, would also increase the confidence that our results incorporate the full range of variation between clinics and clinic days. Similarly, data from additional clinics would increase the generalisability of our results.

Second, there were large amounts of missing data in the clinic attendee movement datasets. Missing data were imputed using multiple imputation, and the effects of the uncertainties in patient times and waiting locations were reflected in the size of the uncertainty bounds around the results. Multiple imputation relies on the assumption that the data are missing at random however, which may not be true for our data sets. We also assume that all clinic attendees visited both files and vitals in turn, and that all attendees waited in a single location per stage, which may not have been the case for all attendees. For these reasons, our results for each

clinic day should be considered to be indicative of the interventions' effects in the clinic, rather than a definitive estimate of the effects of the interventions on each specific clinic day. We may also have missed a number of attendees entirely if they left before the start of data collection, or arrived after the end. The effects of this are likely to have been minimal however, as attendees leaving before the start of data collection could only have spent a small amount of time at the clinic, and attendee numbers were relatively small and fell rapidly after the end of data collection.[11]

Due to the large amounts of missing data in the clinic attendee movement data sets, we were also unable to simulate in any detail the process of queuing for consultations with nurses and doctors, and for the pharmacy. Instead, we simulated a single queue for consultations, using data on clinic leaving times. This is unlikely to have had a substantial effect on the estimates for the majority of interventions, but may mean that we underestimated or overestimated the effects of the appointment systems and CCMDD coverage scale-up interventions. The large amounts of missing data also prevented us from considering the pathways of people who were accompanying patients or attending on the behalf of someone else separately from the pathways of patients, and all clinic attendees are treated as 'patients' in the model. This is unlikely to have had a large effect on the results, as the people accompanying patients are likely to have spent the majority of the time in the same waiting areas as the patients they were accompanying.

Our results will also have been influenced by assumptions made in the parameterisation of the interventions. For instance, we assume that surgical masks offer no direct protection against infection to the wearer of masks, with the reduction in risk coming from mask wearing by infectious people only.[22] If surgical masks also provide some direct protection against infection, then we may have underestimated the effects of the mask wearing intervention.

In a small proportion of runs, the simulated interventions increased the rate of transmission. In the CCMDD and appointment interventions, this occurred through rearrangements in patient pathways making waiting times for some patients higher, or concentrating patients in higher risk waiting areas. These rare outliers reflect day-to-day variation, rather than highlighting a real potential for the interventions to consistently increase risk. For the queue management intervention, increased rates of transmission occurred in model runs where high sampled baseline ventilation rates in waiting areas coincided with a low sampled ventilation rate in the outdoor waiting area in the intervention scenario. In reality, ventilation rates in different areas will be correlated, with both influenced by the same factors such as wind speed,[26] and it is therefore likely that the outlier runs overestimate the true uncertainty.

CONCLUSIONS

To conclude, we show the estimated effects on the rate of *Mtb* transmission to clinic attendees of a range of IPC infections. Median reductions range from 83% for a queue management system with outdoor waiting areas, to 22% from scaling up coverage of CCMDD among ART patients. The majority of the interventions (6/7) achieve reductions of at least 45%, meaning that a range of highly effective conventional and novel IPC intervention options are available, that can be tailored to the local context.

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Contributors NM conceived, designed and conducted the modelling work and wrote the paper. ASK, NM and ADG designed the patient movement data collection, and ASK and IG conducted the data collection. KB conducted the multiple imputation. PB, TAY and IG collected the ventilation data, and PB, TAY and AKD analysed it. KD designed and led the system dynamics modelling to inform intervention choice and design, with contributions from ASK, KK, ADG. ADG, KK, NM, TAY, RW and RMGJH obtained funding. NM is responsible for the overall content as guarantor. All authors read, commented on and approved the paper.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The clinic attendee movement and ventilation data collection received ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. BE082/18), the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town (ref. 165/2018), the Research Ethics Committee of Queen Margaret University (ref. REP 0233) and the Observational/Interventions Research Ethics Committee of the London School of Hygiene & Tropical Medicine (ref. 14872).

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Data availability statement Data are available in a public, open access repository. Data are available upon reasonable request. Model code is available from https://github.com/NickyMcC/WithinClinics. The patient flow datasets will be made available from https://datacompass.lshtm.ac.uk/.

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Supplemental material - Modelling the effect of infection prevention and control measures on rate of Mycobacterium tuberculosis transmission to clinic attendees in primary health clinics in South Africa

Contents

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1 Supplemental methods

1.1 Imputation

1.1.1 Times

Four key times were identified in the pathways that each clinic attendee took through the clinic:

- Arrival time. The time that they first arrived at the clinic. For attendees who arrived after the start of data collection, this was assumed to be the time that their barcode was first scanned. The arrival time was set to missing if the attendee was already present in the clinic before the start of data collection, or if the first time their barcode was scanned was not at a clinic entrance (an external door or compound gate).
- Files time. The time that the attendee obtained their patient file from the clinic reception desk. This was assumed to be the time that their barcode was first scanned at files, provided that it occurred before the first time that they were scanned at vitals or at a consultation room. The time was set to missing if they never scanned at files, or if they scanned at vitals or a consultation room before first scanning at files.
- Vitals time. The time that the attendee has their blood pressure, heart rate, and respiratory rate measured. This was assumed to be the time that their barcode was first scanned at vitals, provided that it occurred before the first time that they were scanned at a consultation room. The time was set to missing if they never scanned at vitals, or if they scanned at a consultation room before first scanning at vitals.
- Leave time. The time that the attendee left the clinic. This was assumed to have occurred at the final time that they scanned their barcode, provided it occurred at a clinic exit point (an external door or compound gate). The leaving time was set to missing for attendees who were still at the clinic at the end of data collection, or if their barcode was never scanned at an exit point.

In a small number of cases, times at files and/or vitals may be missing not because the attendee did not scan their barcode, but because the attendee did not complete that stage. For instance, some attendees who were at the clinic to collect medicine only may have skipped one or both stages. In many clinics, patients on TB treatment can also skip the files and vitals stages. In all eight clinics however, the majority of patients are required to pass through both files and vitals, regardless of their visit reason.

Table S1 shows the number and proportion of attendees with known and missing data for each stage.

				Arrival		Files		Vitals		Leaving			
	Clinic	Clinic closing time	Number of attendees	Known	Missing (arrived early[1])	Missing	Known	Missing	Known	Missing	Known	Missing (left late[2])	Missing
KwaZulu-Natal	1	19:00	417	269 (65%)	130 (31%)	18 (4%)	66 (16%)	351 (84%)	34 (8%)	383 (92%)	248 (59%)	129 (31%)	40 (10%)
	2	17:00	171	130 (76%)	37 (22%)	4 (2%)	62 (36%)	109 (64%)	66 (39%)	105 (61%)	121 (71%)	47 (27%)	3 (2%)
	5	16:30	349	257 (74%)	69 (20%)	23 (7%)	14 (4%)	335 (96%)	38 (11%)	311 (89%)	247 (71%)	89 (26%)	13 (4%)
	6	17:00	377	128 (34%)	63 (17%)	186 (49%)	99 (26%)	278 (74%)	109 (29%)	268 (71%)	174 (46%)	34 (9%)	169 (45%)
Western Cape	8	16:30	69	65 (94%)	2 (3%)	2 (3%)	35 (51%)	34 (49%)	23 (33%)	46 (67%)	55 (80%)	11 (16%)	3 (4%)
	9	16:30	120	56 (47%)	44 (37%)	20 (17%)	34 (28%)	86 (72%)	40 (33%)	80 (67%)	54 (45%)	38 (32%)	28 (23%)
	11	16:30	308	111 (36%)	157 (51%)	40 (13%)	32 (10%)	276 (90%)	24 (8%)	284 (92%)	176 (57%)	43 (14%)	89 (29%)
	12	16:30	144	94 (65%)	39 (27%)	11 (8%)	39 (27%)	105 (73%)	66 (46%)	78 (54%)	121 (84%)	17 (12%)	6 (4%)

Table S1. The number and proportion of attendees with known and missing data for each stage, and clinic closing times [1]The person arrived before the start of data collection. [2]The person left after the end of data collection

Missing times were imputed as interval-censored values, with lower and upper bounds of when the event would have occurred, using a sequential approach. Firstly, arrival times at the clinic were multiply-imputed using 20 imputations. For attendees who arrived before the start of data collection, the lower and upper limits of the time of arrival were set to the clinic opening time and the start of data collection, respectively. For those who arrived after the start, the lower limit was set as the start of data collection, and the upper limit was the time that the attendee was first scanned. Secondly, the time at files was imputed, using the imputed arrival time as the lower bound of the interval and time at vitals (if observed) as the upper limit. If time at vitals was not observed, the upper bound was set to the earliest of the maximum time from arrival to files observed in that clinic, the time of leaving (if observed), end of data collection (if not there at end) or close of clinic (if there at end). Next, the time at vitals was imputed, using the imputed time at files as the lower bound of the interval, and the setting the upper bound to the earliest of the maximum time from files to vitals observed in that clinic, the time of leaving (if observed), end of data collection (if not there at end) or close of clinic (if there at end). Finally, the time of leaving the clinic was imputed, using the imputed time at vitals as the lower bound, and setting the upper bound to the earliest of the maximum time from vitals to leaving observed in that clinic, end of data collection (if not there at end) or close of clinic (if there at end).

Age, sex, clinic, reason for visit, whether there at start/end, and whether the attendee was first scanned in the morning (before 10am) were included in the imputation model. Two sets of 20 imputations were generated. In one, separate lower and upper limits were used for the morning and afternoon visits. This was done as there was some evidence in the empirical data that waiting times were shorter in the afternoons. In the second, the same lower and upper limits were used for all attendees.

For each attendee and imputation, an estimated time at consultations was generated. This was not designed to be an accurate estimate of the exact time that they started any particular consultation,

but instead was used to ensure that the time that attendees spent in waiting areas between vitals and leaving the clinic was not over-estimated. Observations in clinics suggested a mean time per consultation of seven minutes. We assumed that patients have an average of 1.5 consultations per visit, giving a mean length of time spent in consultations of 10.5 minutes. We also assumed that the majority of patients would need a minimum of 3 minutes between starting vitals and starting their first consultation. Finally, the estimated time starting consultations, 'consultation time', could not occur after 'leave time'. The estimated consultation time was therefore set to the latest of 1) attendees leave time – 10.5 minutes, 2) vitals time + 3 minutes, 3) leave time.

The files and vitals stages only take a short amount of time per patient, and in many clinics the patient remains in the files waiting area while their file is being retrieved. The time not spent in the waiting area for files and vitals is therefore considered to be negligible, and is not subtracted from the patients' waiting times in the model.

1.1.2 Locations

We assume that each attendee waits in a single location for each stage of their clinic pathway. That is:

- Between arrival time and files time
- Between files time and vitals time
- Between vitals time and consultation time

Based on observation of the organisation of care and patient flow at each clinic, each stage was assigned a certain area or areas in which individuals would wait to be seen. For each individual, waiting locations for each stage were determined in three steps.

1. For individuals who had a recorded visit to a specific stage:
    a. The location recorded immediately before the stage was used as the most likely waiting location if it was one of the waiting areas associated with that stage.
    b. For stages with only one associated waiting location, individuals who had a recorded visit to a particular stage, but whose immediate previous location was not the waiting area for that stage, were nevertheless listed as having waited in that area, as it was considered likely that their entry and exit to that waiting area had been missed during data collection. For stages with more than one waiting location, individuals were randomised to one of the areas using the method described in point 3 below.
    c. For individuals who visited more than one consultation room, the first consultation room visited and associated waiting area were used.
2. Individuals without a recorded visit to a specific stage (any of filing, vitals, or consultation) were assigned waiting locations based on the organisation of care at the clinic.
    a. In clinics with a single filing and/or vitals stage, and where that stage had only one associated waiting area, all individuals were listed as having waited in the associated waiting area for a particular service. In clinics where a stage had more than one waiting area, individuals were randomised as described below.
    b. In clinics with more than one filing and/or vitals stages (e.g., clinics with separate streams for ‘acute’ and ‘chronic’ patients), individuals were first categorised by stream, based on the reported reason for their visit and by the consultation room they had attended (if recorded). Once again, if a stage had only one associated waiting area (e.g., ‘acute vitals’), all individuals in the appropriate stream (e.g., the ‘acute’ stream) were listed as having waited in that area. If a stage had more than one associated waiting area, individuals were randomised as described below.

3. After the completion of steps 1 and 2, any individuals without recorded waiting locations for any of the three stages were assigned at random to a waiting area associated with that stage. For each stage, the proportions of individuals to be assigned to each associated waiting areas was calculated using the assignments made in steps 1 and 2 above. The remaining individuals were then randomised to the associated waiting areas in the same proportions

A total of 20 attendee waiting location datasets were created for each clinic, incorporating the uncertainty in waiting locations.

The numbers and proportions of attendees with uncertain waiting locations (separated by waiting locations assigned by high probability [step 2, above] and by randomisation [step 3]) are shown in Table S2.

				Number of attendees with uncertain waiting location†, n (%)					
Province	**Clinic**	**Number of attendees**	**Number of waiting areas***	**Files**		**Vitals**		**Consultations**	
				High probability	**Randomised**	**High probability**	**Randomised**	**High probability**	**Randomised**
KwaZulu-Natal	1	417	2	92 (22)	171 (41)	113 (27)	140 (33)	111 (26)	196 (47)
	2	171	4	0	107 (63)	0	89 (52)	0	83 (49)
	5	349	4	142 (41)	183 (52)	290 (83)	0	190 (54)	98 (28)
	6	377	4	268 (71)	0	257 (68)	0	172 (45)	60 (16)
Western Cape	8	69	2	15 (22)	0	34 (49)	0	25 (36)	0
	9	120	2	50 (42)	0	59 (49)	0	60 (50)	0
	11	308	5	275 (89)	0	281 (91)	0	295 (96)	0
	12	144	2	78 (54)	0	61 (42)	0	11 (7.6)	111 (77)

Table S2. The numbers and proportions of attendees with uncertain waiting locations, by clinic and stage. *includes informal waiting areas such as corridors. Informal and formal outdoor waiting areas are not included in this number. †'Uncertainty' separated into those to whom waiting location was assigned based on high probability (step 2 in text) or randomisation (step 3)

1.2 Ventilation data

Empirical data on air changes per hour (ACH) were available from a series of experiments conducted in a range of different rooms in the clinics[1]. Results from a small number of repeat experiments in the same rooms on different days showed that there were large amounts of variation in ventilation rates in the same room between different days. Estimated ACH were available from 84 experiments in 57 rooms (33 experiments in consultation rooms, and 51 in waiting areas) with a typical in-use number of windows and doors open or closed. There was little difference between estimated ACH between consultation rooms and waiting areas (mean 13.1 95% CI 8.2-18.0 and 18.5 95% CI 12.6-24.4, p=0.2), and therefore data from both types of area were used. An exponential distribution was fitted to the estimated rates (Figure 1), and simulated rates in each room were sampled from the distribution for each model run. Estimated air change rates per hour were similar between the data (mean 16.4, median 9.5, IQR 4.3-21.2) and the modelled distribution (mean 15.5, median 9.8, IQR 4.1-23.4).

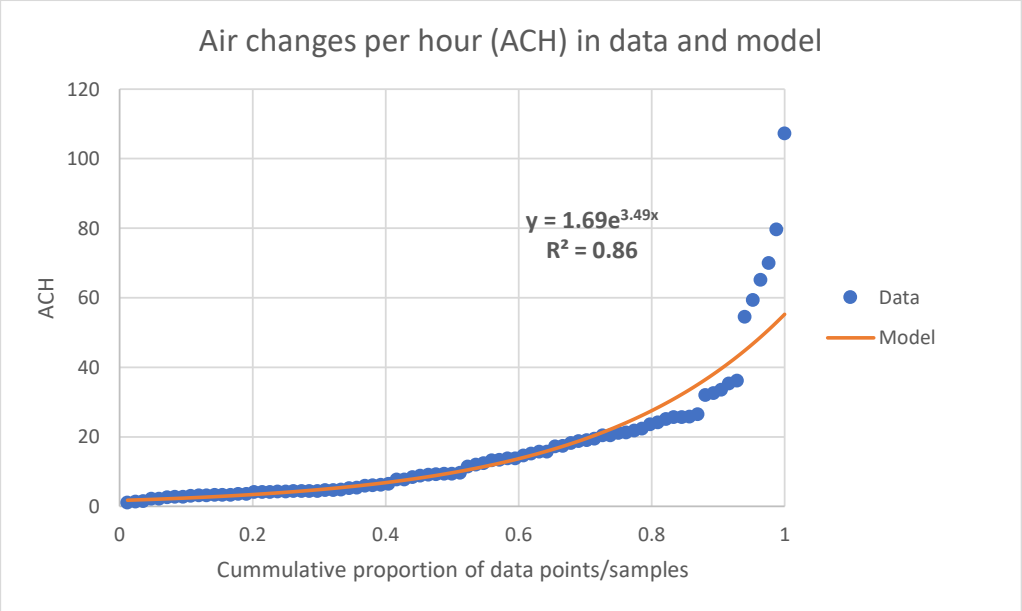

Figure S1. Empirical data on air changes per hour (ACH), and distribution used to generate ACH values in the model

1.3 Model overview

The model was an individual-based model that tracks the movements of attendees through clinics, and *Mycobacterium tuberculosis* infection risk in clinic waiting areas over time, by area and by individual.

In the model, four key (clock) times control each attendee's movement through the clinic, through four corresponding stages: the time they arrive at the clinic, the time they collect their patient file ('files'), the time that their basic measurements are taken ('vitals'), and the time that they start consultations. It is assumed that they leave the clinic immediately after ending consultations, and spend negligible further time in waiting areas. Simulated attendees also each have an assigned waiting area where they wait between each stage (between arrival and files, between files and vitals, and between vitals and consultations). The four key times and three locations were determined, imputed and/or estimated for each attendee, and the complete dataset was used as input to the model. The simulated times and waiting locations remain unchanged in the model from those in the input files, in the baseline scenario and the majority of the intervention scenarios. In the appointment system and CCMDD interventions, the times are changed in the model, and in the queue management system, the waiting locations are changed.

The number of quanta in each waiting area is tracked over time. It is assumed that there is a prevalence of pulmonary tuberculosis among adult and child attendees of 1.0% and 0.016%[2-4] respectively, and that attendees with pulmonary tuberculosis have a mean rate of quanta production of 1.25 per hour[5]. We implement this in the model by giving each adult and child a rate of quanta production of 8.9×10^{-3} and 1.42×10^{-4} per hour respectively.

Movement of clinic attendees was scheduled in the model using continuous time. Updating of quanta in waiting areas and individual's risks was scheduled on a time step, at intervals of *quanta_rate_ts*.

1.4 Key

Model parameter names are written in *italics*, with colour indicating whether the parameter is an input parameter, a parameter with a global model-wide value, calculated from input parameter(s);or an individual-level parameter, which can take a different value for each simulated person, for each simulated waiting area, or for each simulated stage.

1.5 Attendee input file

Each model run for each clinic required an attendee input file, which had a row for each attendee, with the following information:

1. The attendee id
2. The arrival time to be simulated for the attendee (equal to the imputed arrival time for all scenarios except the appointments intervention) (*arrival_time*)
3. The gap in the imputed data between the time they start a stage and the time that the next attendee starts the stage, for each stage (*duration_files*, *duration_vitals*, *duration_cons*)
4. The gap in the imputed data between each of their own stages (*gap_files*, *gap_vitals*, *gap_cons*)
5. The waiting location for each stage (*files_queue_location*, *vitals_queue_location*, *cons_queue_location*)

Each attendee input file contained the same number of attendees for each clinic, with the exception of input files for the CCMDD intervention, where a proportion of attendees were removed (see section 'intervention scenarios'). The gaps between attendees in the input file (*duration_files*, *duration_vitals*, and *duration_cons*) were not affected by the removal of attendees.

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1.6 Movement through clinics

All attendees enter the clinic at *arrival_time*, and set their location to *files_queue_location* (with the exception of the queue management intervention-see Attendee waiting areas). The way that the movement through the other three stages (files, vitals, and consultations) is implemented in the model – the scheduling mechanism – depends on whether the stage is set to be rate limiting or not, for that particular model run. In practice, whether stages are set to be rate limiting or not has no effect on model output for the baseline scenario, or for the majority of intervention scenarios, as in both cases the scheduling mechanisms result in the simulated times at which attendees reach each stage being exactly equal to the corresponding times in the attendee input file. The choice of scheduling mechanism for each stage only effects the results when the number of attendees are changed (CCMDD intervention), or attendee arrival times are changes (appointment systems).

Observations in the clinics suggested that the consultations stage was rate limiting for the majority of patients, with patients queueing for consultations throughout the day. Consultations were therefore assumed to always be rate limiting in the main model runs.

It was not possible to determine whether the files and vital stages were rate limiting in the eight clinics on the day of data collection, due to the large amounts of missing data. Whether a stage is rate limiting or not may also vary over the course of a day. For instance, the files stage may potentially be rate limiting at the start of the clinic day only. Which stages are rate limiting is also to some extent a function of staff allocation. Blockages at files and vitals in particular can be alleviated, through assigning additional staff to those stages. That may not be possible for consultation stages however, where more specific staff skills may be required. For these reasons, we simulated four scheduling scenarios, with both files and vitals simulated as rate limiting, with neither simulated as rate limiting, and with only one simulated as rate limiting.

1.6.1 Scheduling mechanism – rate limiting stages

When the files stage is set to be rate limiting in the model, then the gap between each attendee and the attendee after them (*gap_files*) is kept the same as it is in the attendee input file. The files stage has a variable, *files_status*, that tracks whether there is somebody currently at the stage ('busy'), or whether there is not ('free'). At the start of the model run, *files_status* is set to free.

When *files_status* is set to free, then the next attendee to arrive at the clinic (i.e. finish the preceding stage) immediately starts the files stage, setting *files_status* to 'busy'. When they finish the files stage, after a gap of *duration_files*, then the attendee at the start of the queue for files immediately starts the files stage, and removes themself from the files queue. If there are no attendees in the queue, then *files_status* is set to free.

On arriving at the clinic, if *files_status* is set to busy, attendees add themselves to the end of the files queue.

The scheduling mechanism works in the same way for the vitals and consultation stages, with attendees adding themselves to the queue for the stage after finishing the files and vitals stages respectively.

1.6.2 Scheduling mechanism – non-rate limiting stages

When the files stage is set to be not rate limiting, then the gap between arrival (the preceding stage) and files, *gap_files*, is kept the same as it is in the attendee input file. Upon arriving at the clinic, each attendee schedules their arrival at files, to occur after a gap of *gap_files*.

The scheduling mechanism works in the same way for the vitals and consultation stages, with the preceding stages being files and vitals respectively.

1.6.3 Attendee waiting areas

In the model, between arrival and files, between files and vitals, and between vitals and consultation, attendees wait in *files_queue_location*, *vitals_queue_location*, and *cons_queue_location* respectively.

1.6.3.1 Queue management intervention

The exception to this is when the queue management intervention is simulated. The intervention is described more fully below, but briefly, it is assumed in the intervention that a maximum of only n_1, n_2, and n_3 attendees are allowed to wait inside the clinic before each of files, vitals, and consultations respectively, and that the rest wait in a single outdoor waiting area.

Upon arriving the clinic, simulated attendees check how many attendees are currently waiting inside the clinic for the files stage. If it is less than n_1, then they wait in *files_queue_location*. If it is greater or equal to n_1, then they wait in the outdoor waiting area, and add themselves to the end of a queue.

Each time a attendee reaches files, the length of the queue is checked. If it is greater than zero, then the first attendee in the queue changes their location to *files_queue_location*, and the attendee is removed from the queue.

The process is the same for vitals and consultations.

1.7 Individual characteristics

Individuals in the model are classed as either children (aged <16 years) or adults (aged 16 years or over).

An individual's probability of having pulmonary TB at the time of their clinic visit (*prob_infectious*) is set equal to *prob_infectious_adult* if they are an adult, and *prob_infectious_child* if they are a child.

An individual's breath volume rate (Ls^{-1}) (*breathe_rate*) is set equal to *breath_rate_adult* if they are an adult, and *breath_rate _child* if they are a child.

Individuals in the model wear masks with probability *prob_wear_mask*. This is set to zero in the baseline scenario, and in scenarios where no mask wearing intervention is simulated. Each individual has parameters *own_mask_reduction_out* and *own_mask_reduction_in*, which determine any reduction in the rate that they exhale or inhale quanta respectively, that is attributable to the fact they are wearing a mask. They parameters are set to zero if the individual is not wearing a mask, and to *mask_reduction_out* and *mask_reduction_in* respectively if the individual is wearing a mask.

1.8 Room characteristics

Each room has a room volume, *room_volume*, estimated from empirical data.

Each room has a rate of air change per hour (ACH), *air_change_rate_h*, which is converted into a rate of air change per time step, *air_change_rate_ts*.

For interventions that had no effect on ventilation rates, the same ventilation rates were used for each run for each paired baseline and intervention model run.

See section 'Intervention scenarios' for details of how *air_change_rate_h* was estimated in intervention scenarios that altered ventilation rates.

The number of adults not wearing masks, children not wearing masks, adults wearing masks, and children wearing masks present in each room were tracked by the parameters *count_adults_no_mask*, *count_children_no_mask*, *count_adults_mask*, and *count_children_mask* respectively.

1.9 Infection risk

Each simulated individual tracks the number of quanta in a room that were produced by themself (*own_quanta_in_room*). This parameter is reset to zero each time an individual changes rooms. Each time step, it is updated using EQ1.

$$own\_quanta\_in\_room = (own\_quanta\_in\_room[t-1] * (1 - (air\_change\_rate\_ts)) + prob\_infectious * quanta\_rate\_ts * own\_mask\_reduction\_out) \quad \text{EQ1}$$

The overall number of quanta in the room over time is tracked using equation EQ2

$$\begin{aligned} quanta\_in\_room = {} & quanta\_in\_room[t-1] * (1 - air\_change\_rate\_ts) \\ & + count\_adults\_no\_mask * prop\_infectious\_adult * quanta\_rate\_ts \\ & + count\_children\_no\_mask * prop\_infectious\_child * quanta\_rate\_ts \\ & + count\_adults\_mask * prop\_infectious\_adult * quanta\_rate\_ts * mask\_reduction\_out \\ & + count\_children\_mask * prop\_infectious\_child * quanta\_rate\_ts * mask\_reduction\_out \end{aligned} \quad \text{EQ2}$$

Finally, the risk to each individual each time step is calculated using EQ3

$$current\_risk = (1 - \exp(- (quanta\_in\_room - own\_quanta\_in\_room) * breath\_rate * own\_mask\_reduction\_in / room\_volume)) \quad \text{EQ3}$$

Overall infection risk was calculated as the sum of infection risk for all simulated individuals each time step, over all time they spent in clinic waiting areas

1.10 Intervention scenarios

1.10.1 Opening windows and doors

Empirical data were available from 20 experiments, where air change rates were estimated in the same room on the same day, both with the doors and windows in a typical in-use configuration ('usual conditions'), and with the doors and windows fully open ('max conditions'). For each of these, the ratio of the air change rate in max conditions compared to usual conditions was estimated. An exponential distribution was fitted to these estimated ratios (Figure 2), and simulated ratios in each room were sampled from the distribution for each model run. Estimated ratios were roughly similar

between the data (mean 4.8, median 2.7, IQR 1.4-4.3) and the modelled distribution (mean 3.7, median 2.7, IQR 1.3-5.5).

In the simulated intervention, it is assumed that all doors and windows are kept open at all times.

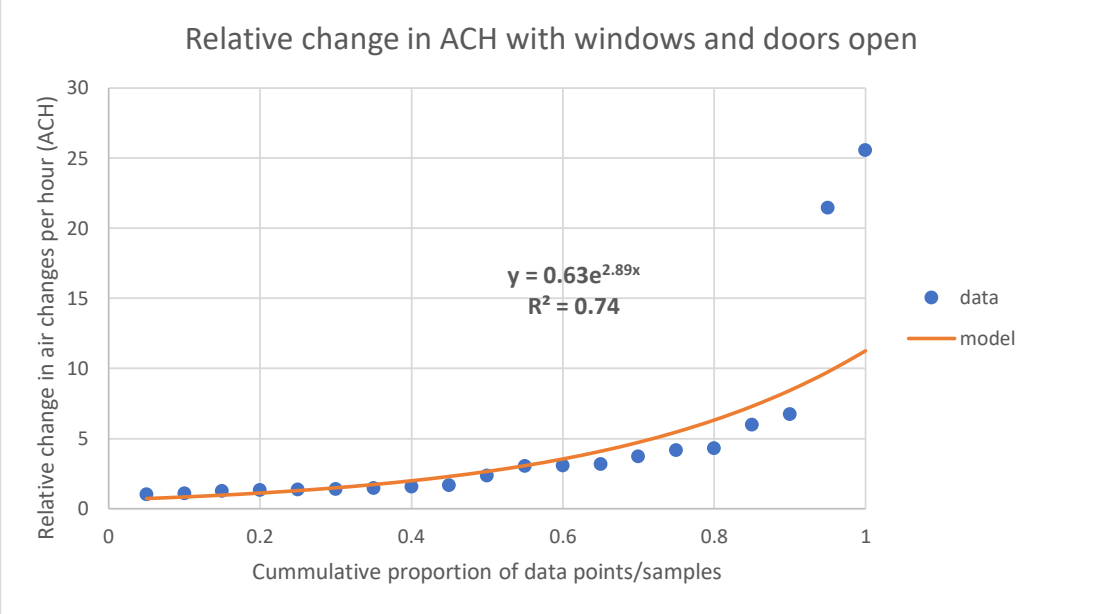

Figure S2. Empirical data on relative change in air changes per hour (ACH) with doors and windows fully open, compared to windows and doors in their typical configurations; and the distribution used to generate the changes in ACH values in the model

1.10.2 Simple clinic retrofits

Retrofits are changes to the building to improve ventilation rates. This could include installing lattice brickwork or whirlybird fans. Due to the large amount of variation between clinic spaces in the types of building retrofits that would be suitable, and the lack of sufficient data on the effects of the retrofits on ventilation and air change rates in different types of spaces, we do not model specific retrofits or packages of retrofits. Instead, we simulate an undefined package of retrofits that are sufficient to increase air changes per hour to a minimum of 12 in all rooms, chosen in line with WHO guidelines[6 7]. This is implemented in the model through increasing *air_change_rate_h* to 12 in all rooms and model runs where the sampled air change rate per hour is below 12.

1.10.3 UVGI systems

We assume in this intervention that appropriate and well maintained ultraviolet germicidal irradiation (UVGI) systems are installed in all indoor clinic waiting areas.

Empirical data from studies of transmission to guinea pigs suggest that UVGI reduces the rate of transmission by 80% (95% CI 64%-88%)[8], equivalent to a ventilation rate of 24 ACH (95% CI 9.9-62)[8]. This is implemented in the model through an additional quanta clearance rate, simulated in the same way as clearance through ventilation. The value of the additional quanta clearance rate is sampled for each waiting area and model run from a split normal distribution with mean 24 and 95% CI 9.9-62%.

1.10.4 Surgical masks wearing by clinic attendees

Based on discussions with health care workers and professionals active in the management of health services in the two provinces we worked in, as well as review of qualitative data collected, we determined that a scenario where 70% of attendees wear surgical masks 90% of the time was plausible. This is implemented in the model as 63% of attendees wearing masks 100% of the time, with the attendees who wear the masks chosen at random each model run.

The relative reduction in the quanta production rate for each mask-wearing attendee each run is assumed to be the same, and the reduction is sampled for each model run from a split normal distribution with mean 75% and 95% CI 56-85%[9].

We assume that masks have no effect on risk of infection for the person wearing the mask[10].

1.10.5 Increased CCMDD coverage

South Africa's Central Chronic Medicine Dispensing and Distribution (CCMDD) programme is designed to allow patients with stable chronic health conditions to collect their medicines from convenient locations, such as local pharmacies[11]. This means that they do not need to queue at clinics unnecessarily. The purpose of this intervention is to increase the coverage of CCMDD and

similar programmes for eligible patients on ART, and to ensure that pick-up points do not require patients to queue at clinics.

In simulating the intervention, we focus on ART patients only, as they make up a large proportion of patients attending for non-tuberculosis related chronic care (399/493, 81%, in the empirical datasets), and because few data were available on patients with other chronic conditions such as diabetes.

Visit reason was collected from all attendees visiting the clinics on the data collection days, with 'Chronic care: HIV/ART' being one of the reported reasons. We assume that some of the clinic visits with 'Chronic care: HIV/ART' being listed as the main visit reason would not be needed with the increased implementation of CCMDD. We therefore remove a proportion, *p*, of those attendees from the model.

In Western Cape clinics, there was an error during data collection, with the majority of patients who attended for HIV/ART related reasons having their main visit reason recorded as 'Acute care: minor problems'[12]. The correct proportions of adult male and female patients attending for HIV/ART related reasons were therefore estimated for Western Cape clinics from the proportions in the KwaZulu-Natal clinics, adjusted for the lower prevalence of HIV and ART coverage in Western Cape[13]. Adult Western Cape 'Acute care: minor problems' patients were then assigned at random, for each clinic and model run, to have attended for HIV/ART related reasons, to reach the desired proportion of male and female patients attending for HIV/ART related care.

2.8% of attendees report their visit reason as attending on behalf of somebody else. We assume that a proportion, *p*, of those visits would also need not occur under a scaled up CCMDD intervention.

For 69/120 (59%) people who reported their visit reason as accompanying an adult, and 72/179 (40%) people who reported their visit reason as accompanying a child, the visit reason of the person that they were accompanying could be determined. For accompanying people for whom the visit

reason of the person they were accompanying could not be determined, they were randomly assigned to be accompanying an HIV/ART patient each model run, with probability equal to the proportions where it could be determined, by clinic and whether they were accompanying an adult or a child. A proportion, *p*, of the visits of people assigned to accompanying someone attending the clinic for HIV/ART care were assumed not to have been needed under the intervention scenario.

The proportion, *p*, was determined using data from a social contacts survey of 1704 adults living in the catchment areas of two clinics in KwaZulu-Natal[14]. Respondents were asked to report the number of times that they had attended a clinic (for their own health) in the past six months. Self-reported HIV-positive people (of who 480/493 (97%) reported being on ART), reported a mean of 8.8 clinic visits per year, compared to 4.1 by HIV-/unknown. That is, an excess of 4.1 (95% CI 3.6-4.5) visits per year, controlling for age and sex, which we attribute to ART appointments. We assume that 92% (95% CI 84-95%) of people could have their ART appointments reduced to once every 6 months (the estimated proportion of people on ART who were virally suppressed 2019[13]), and that the remaining 8% of people need monthly ART appointments. This gives us a 31% reduction (IQR 22-34%) in HIV/ART care visits. For each clinic and model run, the number of excess visits and proportion of ART patients who are virally supressed are sampled from the relevant normal distributions, and *p* is calculated.

We implicitly assume that CCMDD pickup either occurs at a location away from the clinic; or requires patients to spend a negligible amount of time inside the clinic, without having any effect on the delays for other patients.

Ethical approval for the social contacts survey was granted by the Biomedical Research Ethics Committee (REC) of the University of KwaZulu-Natal (UKZN) (BE662/17) and the London School of Hygiene & Tropical Medicine (14640).

1.10.6 Queue management system and outside waiting areas

Empirical data show that clinic waiting areas are often crowded, and that in many clinics attendees wait in unsuitable areas such as corridors[12]. Conversations with clinic staff suggested that this is partly due to patient concerns that if they wait in other areas, they may not hear their name being called, and may miss their turn. This intervention therefore combines a large, covered outdoor waiting area with a queue management system, such as numbered tickets or an electronic tracking system.

We assume in the model that only the next n_1, n_2, and n_3 attendees due to be seen at files, vitals, or for consultations respectively are allowed to wait inside the clinic. At smaller clinics, with fewer than 300 attendees on the day of data collection, n_1=5, n_2=5, and n_3=10. At larger clinics, n_1=10, n_2=10, and n_3=20. Once allowed inside the clinic, attendees are assumed to wait in the same location for each stage as they wait in the baseline scenario.

The volume of the outdoor waiting area is assumed to be equal to the sum of the volume of the existing clinic waiting areas. The ACH is the outdoor waiting area is drawn from a uniform distribution between 52 and 70 ACH for each clinic and model run[15]

1.10.7 Appointment systems

In this intervention, we simulate an appointment system to reduce clinic overcrowding, through spacing out the arrival times of patients. As date-time appointment systems were already in place in some form in the Western Cape clinics on the day that the attendee data were collected, we only model the appointment intervention in the KwaZulu-Natal clinics.

We assume that appointments are given in 10-minute slots (i.e. a patient could be assigned 10:00 or 10:10, but not 10:05), between 9am and 1.50pm, and that patients arrive between 0-10 minutes before their appointment (sampled from a uniform distribution for each attendee). Once arrived at the clinic, simulated attendees are seen by clinic staff as soon as capacity allows, even if it is before

their appointment time. Arrival times are not changed for attendees who are not assigned appointments, and they enter the simulated queues at the time that they arrive at the clinic.

Patients were assumed to be acute patients if their main reported visit reason was 'Acute care: minor problems' or 'Acute care: 24-hour emergency unit', and chronic otherwise. As with the CCMDD intervention, a proportion of patients at Western Cape clinics whose visit reason was recorded as 'Acute care: minor problems' was assumed to have visited for HIV/ART care – i.e. chronic care. In the model, appointments are given to all adult chronic patients. The first N acute patients are assumed to be seen the same day, as well as any children aged <16 years. The remaining adult acute patients are given appointments.

N is calculated for each clinic and model run by multiplying the total number of attendees counted on the day of data collection by the proportion of the total daily clinic time (length of time set aside for drop-in acute patients only plus the length of time that the clinic assigns appointments) that is set aside to see patients without appointments in the morning. N is then multiplied by a number drawn from a random uniform distribution between 0.75 and 1.25 for each clinic and model run, to reflect day-to-day fluctuations in the numbers of patients.

For 69/120 (59%) people who reported their visit reason as accompanying an adult, and 72/179 (40%) people who reported their visit reason as accompanying a child, the visit reason of the person that they were accompanying could be determined. For accompanying people for whom the visit reason of the person they were accompanying could not be determined, they were randomly assigned to be accompanying an acute or chronic patient each model run, with probability equal to the proportions where it could be determined, by clinic and accompanying adult or child. Accompanying people were given appointments or seen the same day based on the visit reason of the person they were accompanying.

It is assumed that there is no risk of transmission to or from attendees while they are receiving their appointment slots, reflecting the fact that many appointments could be arranged on a prior visit or

by telephone, and that the remaining appointments could be arranged quickly in a well ventilated or covered outdoor location, with the attendees rapidly leaving the clinic after receiving their appointment.

In the appointment system intervention, when the files stage in considered to be rate limiting (see section 'Movement through clinics'), the gap between attendees at files is reduced by 50%. This is done to incorporate a plausible reduction in the mean time taken to find files that might be achieved by pre-retrieval of files for patients with appointments.

1.11 Input parameter values

Parameter	Scenario	Description	Value	Source
prob_infectious_adult	All	Proportion of adults visiting the clinic that have pulmonary TB	0.010	Clinic prevalence survey[4]
prob_infectious_child	All	Proportion of children visiting the clinic that have pulmonary TB	0.00016	Clinic prevalence survey[4], adjusting for lower proportion of smear+ disease in children[2], and lower incidence of disease[3]
quanta_rate_hour	All	Rate of quanta production per hour for individuals with pulmonary TB	1.25	Andrews *et al* (2014)[5]
breath_rate_adult	All	Breath volume rate of adults (lh^{-1})	480	Rudnick and Milton (2003)[16]
breath_rate_child	All	Breath volume rate of children (lh^{-1})	288	Rudnick and Milton (2003)[16], adjusting for lower breathe volume in children[17]

quanta_rate_ts	All	Time step for updating quanta and infection risk estimates (seconds)	10	NA
min_ACH	Retrofits	Minimum air changes per hour	12	WHO guidelines[6 7]
mask_reduction_out	Masks	Relative rate of quanta exhalation in individuals with pulmonary TB who wear a mask compared to those who don't	0.25 (0.15-0.44)	Dharmadhikari *et al* (2012)[9]
mask_reduction_in	Masks	Relative rate of quanta inhalation in individuals without pulmonary TB who wear a mask compared to those who don't	1	MacIntyre (2015)[10]
prob_wear_mask	Masks	Proportion of attendees who wear a surgical mask	0.9 * 0.7 = 0.63	Expert opinion
UVGI_rate	UVGI	Rate of quanta clearance due to UVGI, given in units of the equivalent air changes per hour	24 ACH (95% CI 9.9-61.7)	Mphaphlele (2015)[8]

files_indoor_number	Queue management	Number of attendees allowed to wait inside the clinic for the files step	Clinics 2, 8, 9, 12: 5; Clinics 1, 5, 6, 11: 10	Expert opinion
vitals_indoor_number	Queue management	Number of attendees allowed to wait inside the clinic for the files step	Clinics 2, 8, 9, 12: 5; Clinics 1, 5, 6, 11: 10	Expert opinion
consultation_indoor_number	Queue management	Number of attendees allowed to wait inside the clinic for the files step	Clinics 2, 8, 9, 12: 5; Clinics 1, 5, 6, 11: 10	Expert opinion
outdoor_waiting_area_ACH	Queue management	Air changes per hour (ACH) in the outdoor waiting area	52-70	Escombe *et al*[15]
excess_visits_ART	CCMDD	Number of excess clinic visits per year for people on ART, compared to people not on ART	4.1 (95% CI 3.6-4.5)	Empirical social contact data[14]
prop_viral_supressed	CCMDD	Proportion of patients on ART who are virally supressed	92% (95% CI 84-95%)	AIDSinfo[18]

2 Supplemental results

2.1 Sensitivity analysis

Simulating consultations as a non-rate limiting stage reduced the estimated reduction in the rate of transmission to 15% (IQR 8.7-23%) in the CCMDD scale-up intervention, and 24% (IQR 13-47%) in the appointments intervention (Figure S3). It had no effects on the estimates for any other intervention.

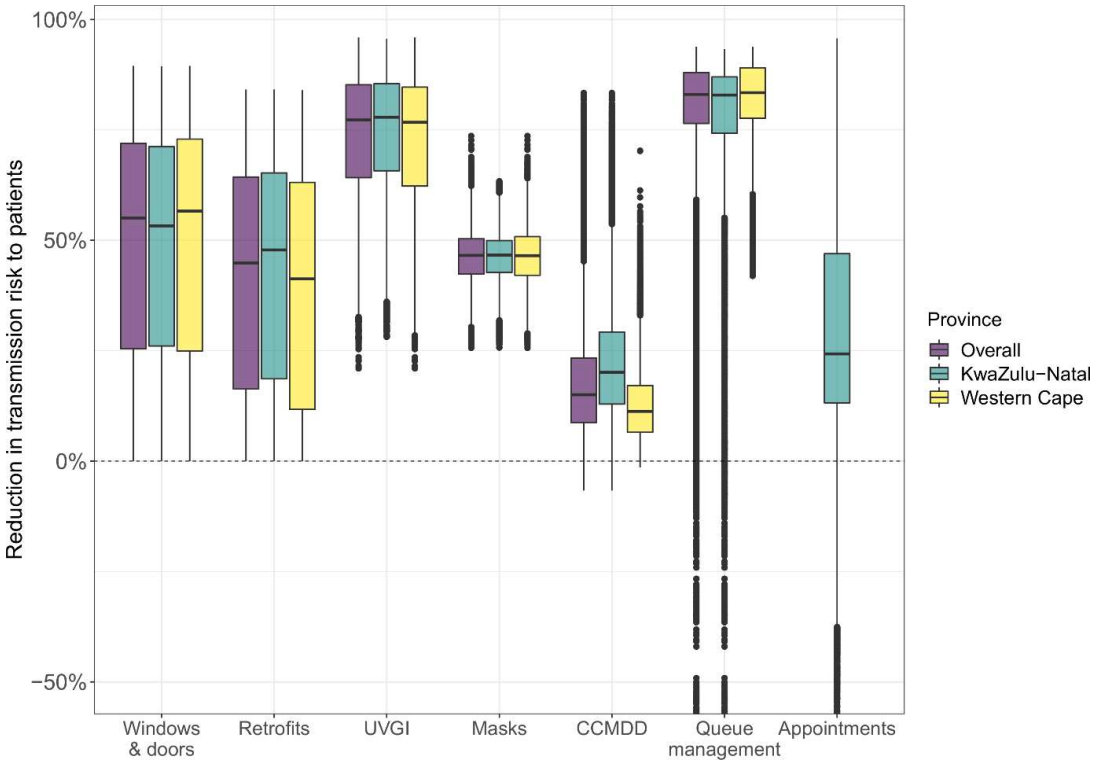

Figure S3. Estimated reduction in the rate of *Mycobacterium tuberculosis* transmission to attendees in clinics, by province and intervention, when consultations are included in the model as a non-rate limiting stage. The central line indicates the median, the box range the interquartile range (IQR), the whiskers the most extreme value within 1.5 * IQR from the box, and the points outlying values. In the queue management intervention in KwaZulu-Natal, 1% of points were below -50%, with a minimum of -162%. In the appointments intervention in KwaZulu-Natal, 0.28% of points were below -50%, with a minimum of -150%. These points are not shown on the graph. The

appointment system intervention was not modelling in Western Cape, due to the presence of existing appointment systems. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

2.2 Intervention impact by clinic

Figure S4 shows the effect of the interventions on the rate of transmission to attendees by clinic.

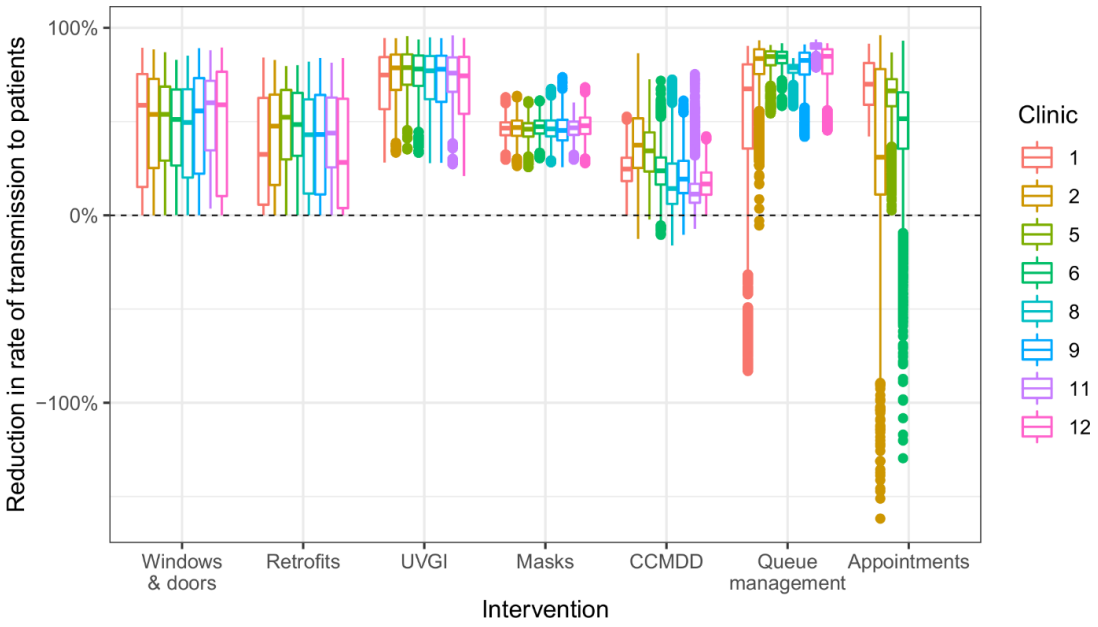

Figure S4. Estimated reduction in the rate of *Mycobacterium tuberculosis* transmission to attendees in clinics, by clinic and intervention. The central line indicates the median, the box range the interquartile range (IQR), the whiskers the most extreme value within 1.5 * IQR from the box, and the points outlying values. The appointment system intervention was not modelling in Western Cape, due to the presence of existing appointment systems. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

2.3 Attendee numbers and rate of transmission over time

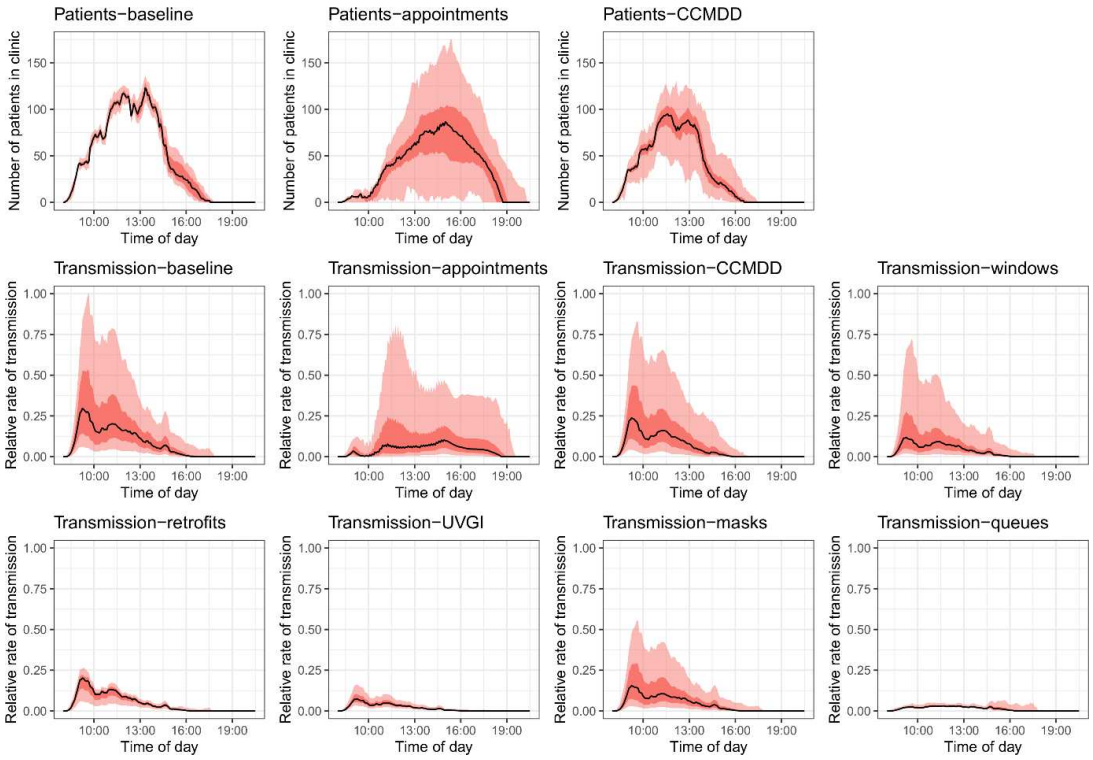

Figure S5. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 2. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine

Dispensing and Distribution.

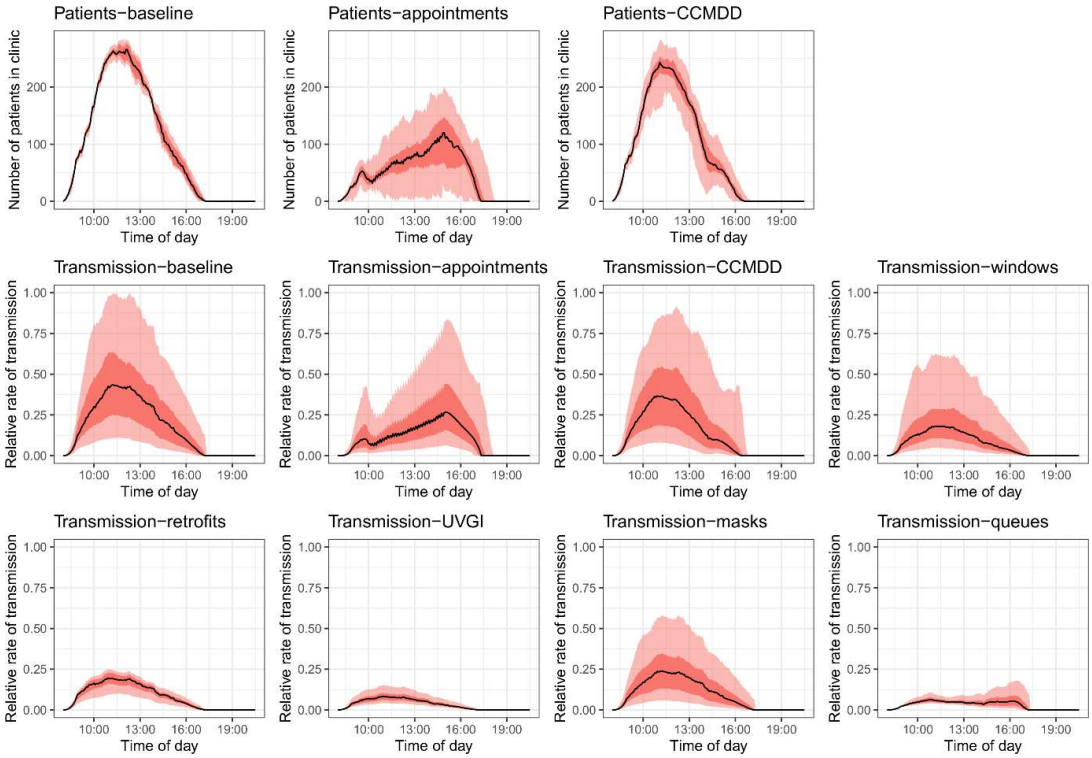

Figure S6. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 5. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

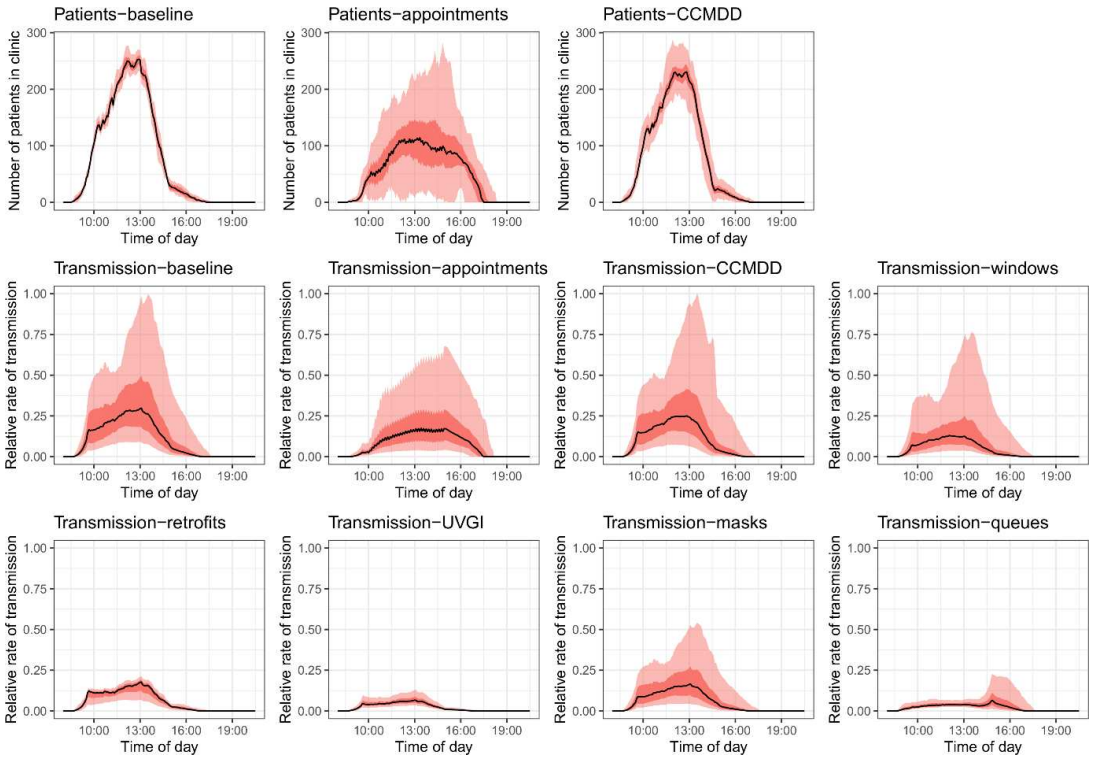

Figure S7. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 6. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

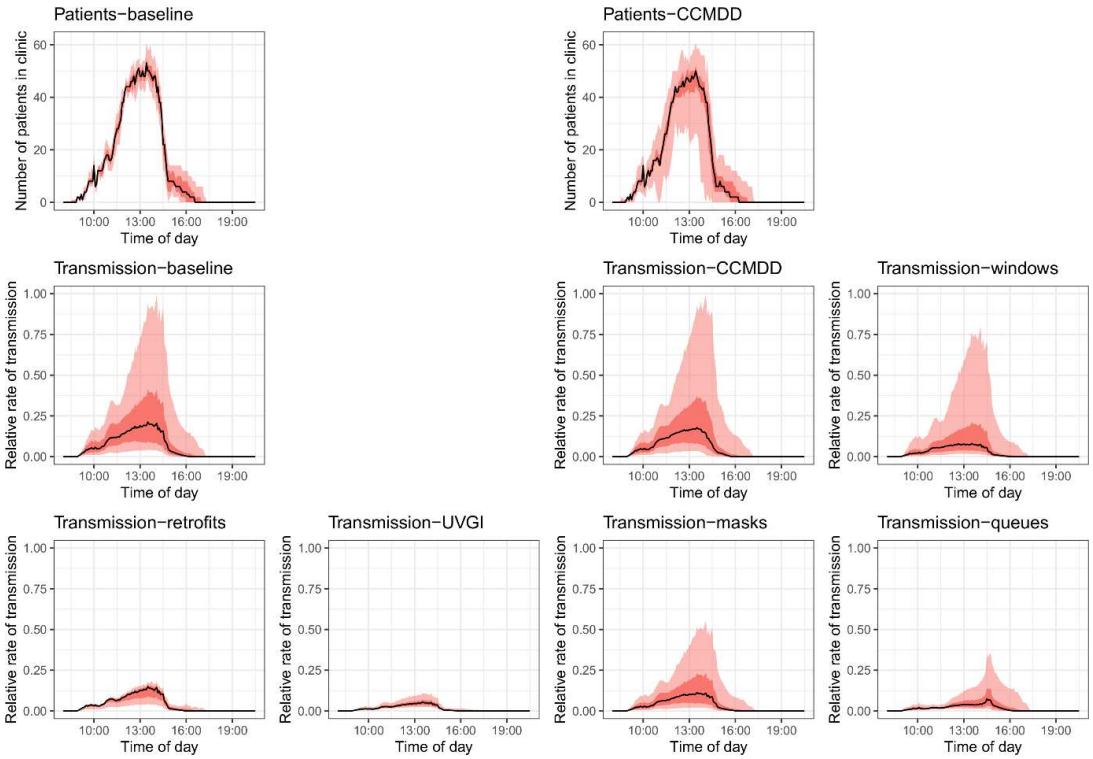

Figure S8. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 8. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

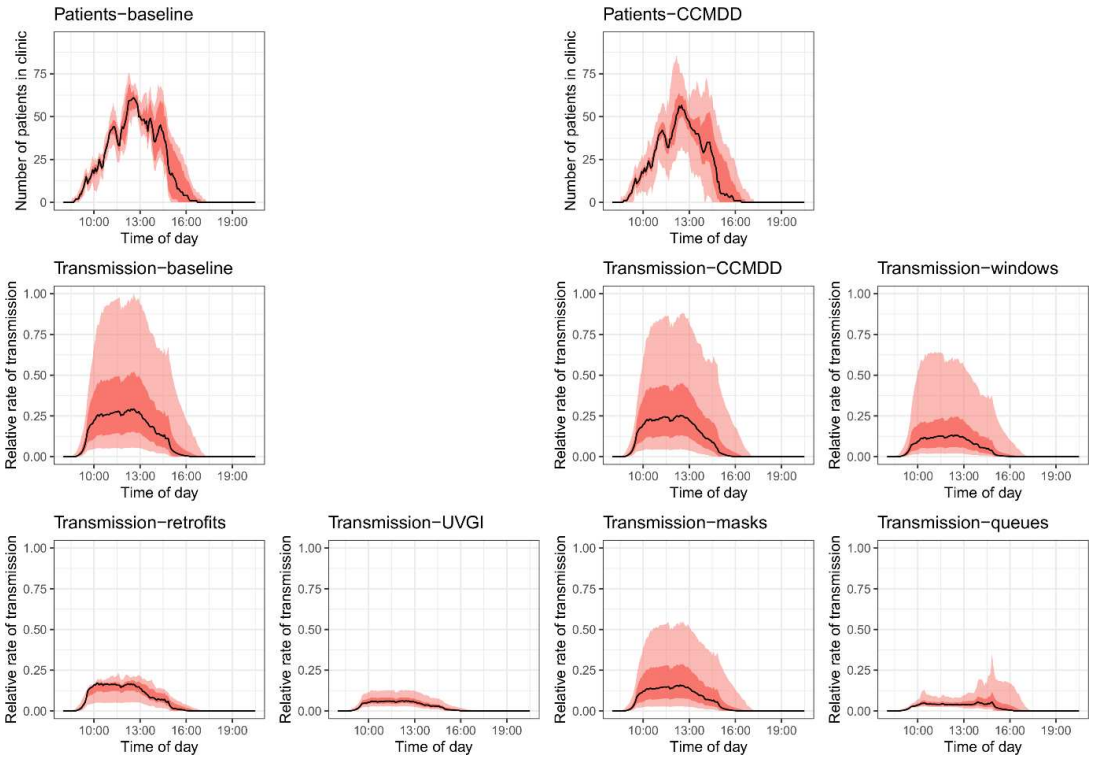

Figure S9. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 9. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on patient numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

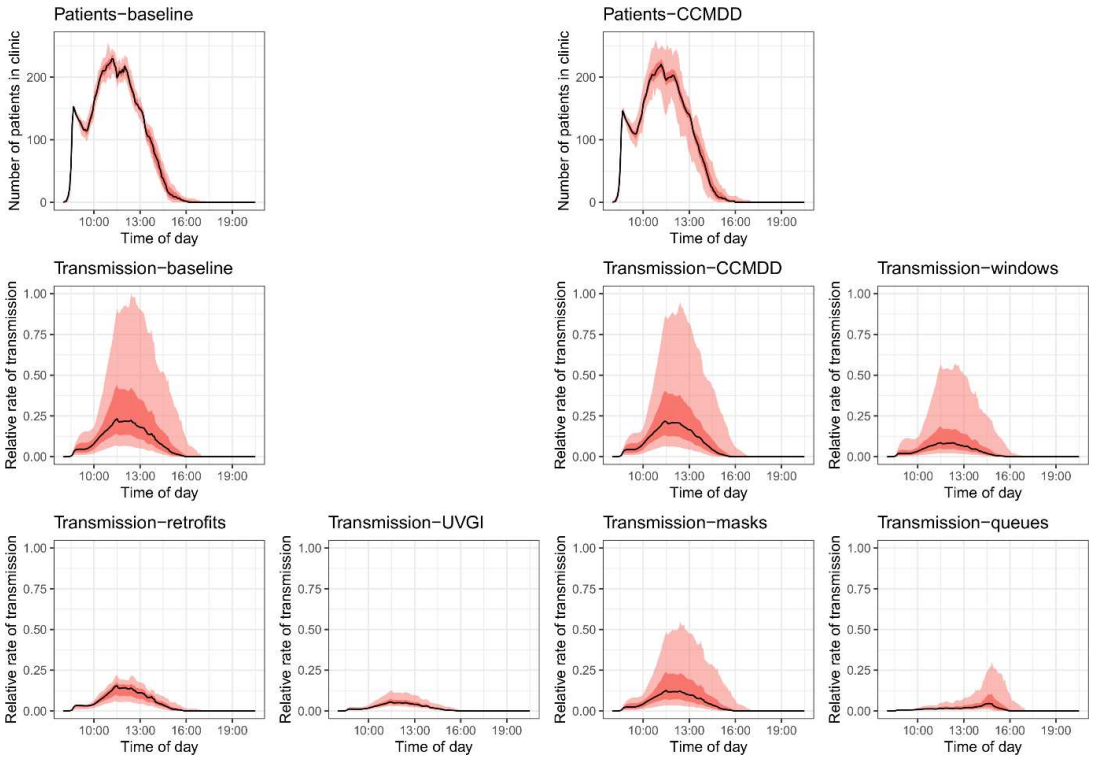

Figure S10. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 11. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

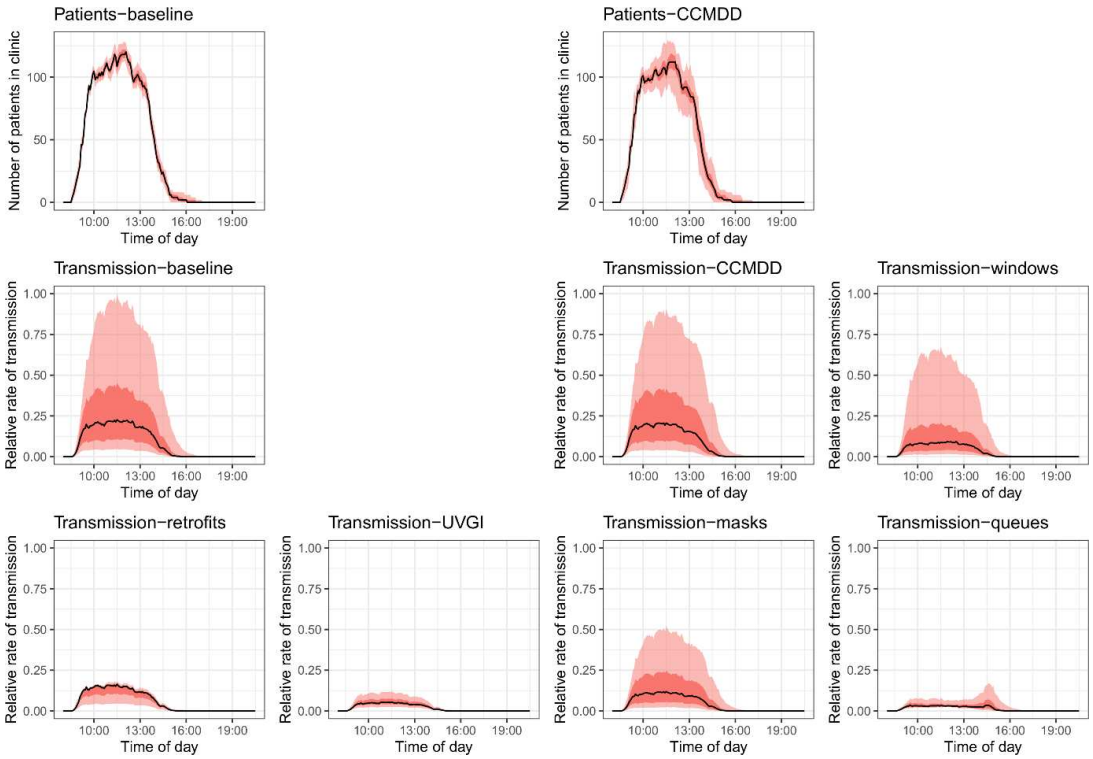

Figure S11. Number of attendees in the clinic over time in the baseline, appointments, and CCMDD interventions, and the mean rate of transmission to each attendee in the clinic over time in all scenarios, for clinic 12. The black line shows the median result, the dark red band the interquartile range, and the light red band the 95% plausible range. For interventions where a plot of the number of attendees over time is not shown, the intervention has no effect on attendee numbers. Transmission rates are relative to the highest transmission rate in any scenario at any point in time. UVGI stands for ultraviolet germicidal irradiation, and CCMDD for Central Chronic Medicine Dispensing and Distribution.

2.4 Median clinic visit durations

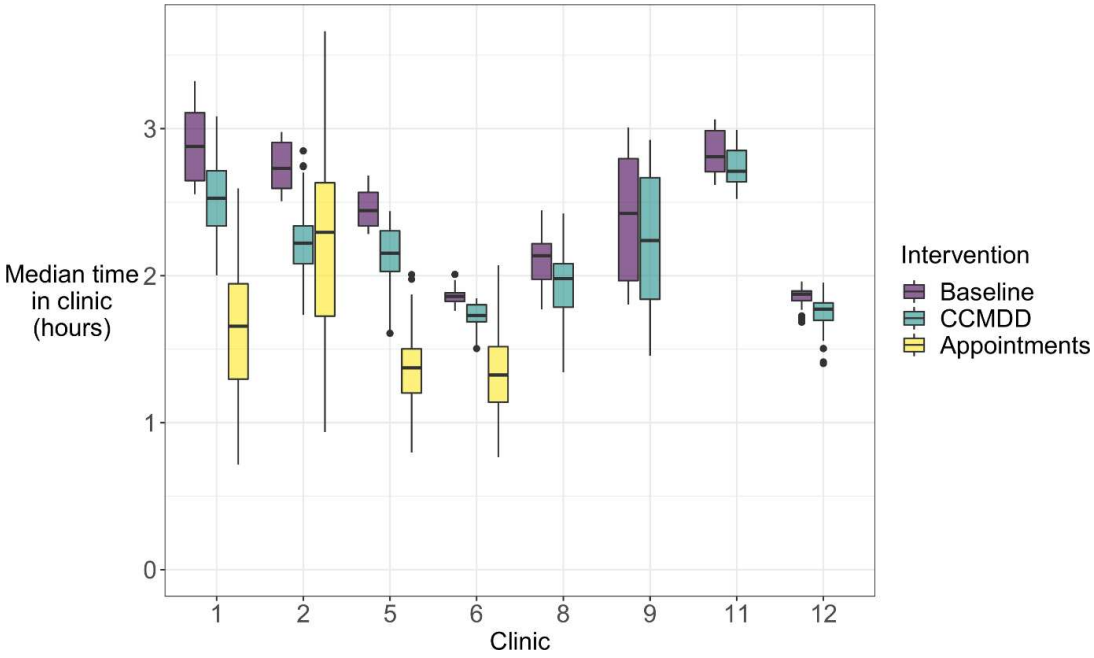

Figure S12. Median attendee times in clinic, by clinic and intervention. The boxplots show the distribution of the median attendee time in the clinic for each model run (i.e. not the duration of time spent in the clinic by each attendee). The central line indicates the median across model runs, the box ranges the interquartile range (IQR), the whiskers the most extreme value within 1.5 * IQR from the box, and the points outlying values. CCMDD for Central Chronic Medicine Dispensing and Distribution.

3 Supplemental acknowledgements

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